PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

Francesco MAKOVEC, et al.

Docket No: Q91867

Appln. No.: 10/562,013

Group Art Unit: 1621

Confirmation No.: 2981

Examiner: Sudhakar Katakam

Filed: December 23, 2005

For: METHOD FOR THE PREPARATION OF CRYSTALLINE DEXLOXIGLUMIDE AND PRODUCTS OBTAINED

DECLARATION UNDER 37 C.F.R. § 1.132

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Dr. Francesco Makovec, am a co-inventor of the presently claimed subject matter in the above-identified application;

THAT I am familiar with the rejection of claims 1-2 and 4-15 as being unpatentable for obviousness over U.S. 5,130,474 ("Makovec") in combination with US 5,314,506 ("Midler") and US 7,122,083 ("Green"); and

THAT the following experiments were conducted by me or under my supervision to demonstrate the differences and superiority of the product obtained by the present invention.

EXPERIMENT:

Crystallization of CR2017 (10g) (preparation K/2344-1)

The compound CR2017 lot D/4740 (10g; molecular weight 461.38) was suspended in 120 ml of a solution of EtOH-water 1:2. The solution was heated to reflux until complete dissolution. Then, the solution was allowed to cool down to room temperature for two hours

(an opalescent mass was obtained); thereafter the solution was further cooled in an ice bath for 16 hours. A semi-crystalline solid which was slightly sticky is filtered and then dried on P_2O_5 for 24 hours. After 24 hours, a second solid is precipitated which is also dried on P_2O_5 for 24 hours.

Yield: 4.5 g of solid A and 1 g of solid B (total 5.5g; 55%)

TLC: (butanol: acetic acid :water (5:2:2)) according to specification

(isoamilic alcohol : acetone : water (5:2:1)) according to specification

IR: according to specification.

The product of Makovec obtained by crystallization from H_2O-EtOH (ratio 2:1) and the product of the present invention obtained by crystallization from isopropyl ether according to Example 1 were analyzed using X-ray diffraction.

From Fig. 1 below, it can be seen that even though the diffraction pattern is similar between the two products, the sample crystallized from H_2O-EtOH (2:1) ("Makovec") contains a much higher percentage of amorphous material (68%). The high percentage of amorphous material makes the obtained powder hygroscopic, sticky, and light with poor flowability, whereby such product is not suitable for preparing pharmaceutical oral formulations, specifically tablets.

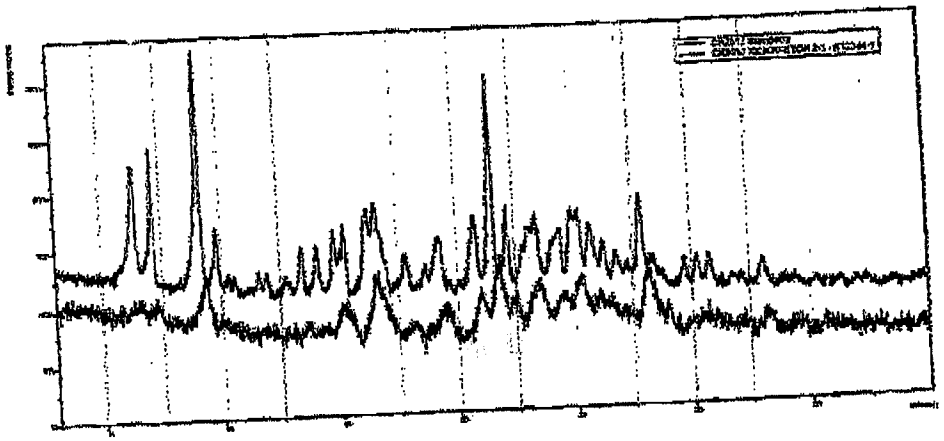

Fig. 1 Comparison between XRPD patterns of CR2017 (H_2O-EtOH (2:1)) and present invention.

This shows that the method of the present invention allows for a product that exhibits unexpectedly superior properties.

I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: Sept. 10, 2008

Dr. Francesco Makovec